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09/884,465	06/20/2001	Josee Hamel	55190-044	9640

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EXAMINER
FORD, VANESSA L

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/884,465	Applicant(s) HAMEL ET AL.	
	Examiner Vanessa L. Ford	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *1-17, 20-24 and 26-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,19,25 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8,13,16* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group III, claims 18-23, 25 and 34 and species SEQ ID NO: 332 (from Table H) filed on October 23, 2002 is acknowledged. Claims 1-17, 24 and 26-33 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being to a non-elected invention. Claims 20-23 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being to a non-elected species.

The traversal is on the grounds that Groups III and IV are not independent and distinct, therefore the examination of the entire application does not constitute a serious burden. Applicant also transverses the election of a single SEQ ID NO. to be examined. These arguments have been fully considered but are not found to be persuasive for the reasons below:

First, the classification system has no statutory recognition whether inventions are independent and distinct. For example, each class and subclass is comprised of numerous completely independent and distinct patented inventions.

Second, MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required.

The term "distinct" is defined to mean that two or more subjects as disclosed are related, for example as product and method of use, etc., but are capable of separate manufacture, use or sale as claimed, and are patentable over each other (see MPEP

802.01). In the instant situation, Group III is drawn to isolated polypeptides. Group IV is drawn to chimeric polypeptides. The inventions of Groups III and IV are drawn to distinct inventions which are separate products.

Classification of the subject matter is merely one indication of the burdensome nature of the search. The literature search, particularly relevant in this art, is not co-extensive, because for example, Groups III and IV are drawn to products , which are structurally distinct. The elected invention also encompasses numerous amino acid sequences represented by numerous SEQ ID Nos. Each SEQ ID NO. that is encompassed by the elected invention are structurally independent and distinct each from the other. Clearly different searches and issues are involved in the examination of each Group as well as the search and examination of each structurally distinct amino acid sequence.

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. Claim 34 is directed to non-statutory subject matter. Claim 34 is rejected under 35 U.S.C. 101 because of the ~~phase~~ phrase "use". Use is a directed to non-statutory class of invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 18-19, 25 and 34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses SEQ ID NO: 332 (elected sequence), which correspond to an isolated protein from *Streptococcus pneumoniae*. The claims are directed to encompass amino acid sequences that correspond to sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a recited degree of identity (similarity, homology), and so forth. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification

does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO:332 (elected sequence), the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the

invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a protein requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a protein requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the protein itself." Id. at 1170, 25 USPQ2d at 1606.

Therefore, only SEQ ID NO: 332 but not the full breadth of the claim (or none of the sequences encompassed by the claim) meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

4. Claims 18-19, 25 and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated *Streptococcus pneumoniae* polypeptide that has the amino acid sequence as set forth in SEQ ID NO: 332 (elected sequence), does not reasonably provide enablement for epitope bearing

portions of the polypeptide having the amino acid sequence as set forth in SEQ ID NO: 332.

The claims are directed to encompass amino acid sequences that correspond to sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a recited degree of identity (similarity, homology), and so forth.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification teaches that the antigenic/immunogenic fragments of invention include one or more epitopic regions (page 15). The specification does not disclose, which amino acids are involved in the claimed epitope bearing portions of the *Streptococcus pneumoniae* polypeptide as set forth in SEQ ID NO:332 nor does the specification provide guidance as to how many location changes (i.e. deletions) can be used to produce an epitope bearing portion of SEQ ID. NO:332. No working examples are shown containing the missing information. There is no guidance provided as to which amino acids can be deleted and still have the epitope retain its biological function. The specification provides essentially no guidance as to which of the essentially infinite possible choices is likely to be successful. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of epitopesn broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species.

Without such information, one of skill in the art could not predict which deletions, would result in the desired epitope. Since the amino acid sequence of the protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity requires a knowledge with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expected intolerant to modification) and detailed knowledge of the ways in which the protein's structure relates to function. However, the problem of the prediction of protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and outside of the realm of routine experimentation.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to epitope bearing portions of a

polypeptide has an amino acid sequence as set forth in SEQ ID NO:332 having claimed functional features, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). One of skill in the art would require guidance, in order to make of the claimed *Streptococcus pneumoniae* polypeptide in a manner reasonable in correlation with the scope of the claims. Without proper guidance, the experimentation is undue.

The Applicant has not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of deletions and epitopes of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made in the protein's structure and still maintain activity is unpredictable and the experimentation left those skilled in the art is unnecessarily and improperly, extensive and undue. See Amgen Inc v Chugai Pharmaceutical Co Ltd. 927 F 2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Exparte Forman, 230 U.S. P.Q. 546(Bd. Pat=. App & int. 1986).

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to make and use the claimed invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Claim 18 recites "an isolated polypeptide comprising a member chosen from" which renders the claim indefinite by reciting improper Markush language. Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B and C." See Ex parte Markush, 1925 C.d. 126 (Comm'r Pat. 1925). It is unclear to which polypeptides the claim is referring?

6. Claim 18 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 18 recites "epitope bearing portion" it is unclear as to what the applicant is referring?

7. Claim 18 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 18 recites "capable of" it is unclear as to what the applicant is referring?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

It should be noted that the Examiner is viewing the claimed isolated polypeptide to read on "an epitope-bearing portion of a polypeptide having an amino acid sequence" as set forth in SEQ ID NO:332 (elected sequence).

8. Claims 18-19, 25 and 34 are rejected under 35 U.S.C. 102(b) as anticipated by *(WO 98/18930, published May 7, 1998).*

Claims 18-19, 25 and 34 are drawn to an isolated polypeptide and vaccine comprising the isolated polypeptide and a pharmaceutically acceptable carrier, diluent or adjuvant.

Kunsch et al teach epitope beâring peptides, polypeptides and vaccines comprising the epitope bearing peptides (pages 4-5 and pages 25-26). Kunsch et al teach an polypeptide as set forth in SEQ ID NO: 66 which comprises epitopes which correspond to several epitopes bearing portions of the polypeptide as set forth in SEQ ID NO: 332 (elected sequence) (see the highlighted amino acids sequences on page 62). Kunsch et al teach that vaccines of the invention comprise one or more of the polypeptides or polypeptide fragments of the invention (page 36). Kunsch et al teach that the vaccine compositions may include salts, buffers, adjuvants or other substance which are desirable for improving the efficacy of the composition (pages 39-40).

Since the Office does not have the facilities for examining and comparing applicant's vaccine and polypeptide fragment with the vaccine and polypeptide fragment of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the vaccine and polypeptide fragment of the prior art does not possess the same material structural and functional characteristics of the claimed vaccine and polypeptide fragment). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Status of Claims

9. No claims allowed.

Conclusion

10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
March 31, 2003

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